IN THE SPECIFICATION

Page 1, between the title of the invention and the first line of the text, insert the following:

CROSS-REFERENCE TO RELATED APPLICATION

This Application is a Section 371 National Stage Application of International Application No. PCT/FR2004/01962, filed July 22, 2004 and published as WO 2005/020974 on March 10, 2005, not in English.

FIELD OF THE DISCLOSURE

Please replace the paragraphs appearing on page 1, lines 1-4 with the following amended paragraphs:

This ~~invention~~ disclosure relates to the pharmaceutical domain.

More precisely, the ~~invention~~ disclosure relates to a novel use of polyamine-poor food compositions for the production of a food that may have therapeutic effects.

Page 1, after line 7, insert the following heading:

BACKGROUND OF THE DISCLOSURE

Please delete the paragraphs starting on page 2, line 4 and ending on page 3, line 2:

~~The purpose of this invention is to propose an alternative to the use of such antagonists to efficiently inhibit functioning of the NR2B sub-unit of NMDA receptors, in other words without inducing any major undesirable effect.~~

~~Thus, one purpose of this invention is to propose a therapeutic agent that could be used to treat neuro-degenerative diseases induced by stimulation of this sub-unit.~~

~~Another purpose of this invention is to propose a therapeutic agent capable of blocking the development of increased sensitivity to pain, memorisation of pain and~~

~~consequently the development of chronic pain.~~

~~In particular, one purpose of this invention is to propose a therapeutic agent capable of restoring the analgesic effects of opioid substances by opposing the tolerance process.~~

~~Opioids such as morphine are powerful and widely used analgesics. However, they also cause dose-dependent development of hypersensitivity to pain in the long term (so-called pronociceptive effect) that can cause long-term hyperalgesia (exaggerated painful sensation to a nociceptive stimulus) and allodynies (painful sensation to a non-nociceptive stimulus). This increase in sensitivity to pain may be caused by the development of tolerance to analgesic effects (Simonnet et al., NeuroReport, 2003, 14, 1-7).~~

Please replace the paragraph appearing on page 3, lines 3-8 with the following amended paragraph:

SUMMARY

~~These purposes are achieved with~~An embodiment of the invention ~~that~~ relates to the new use of a food composition for human consumption containing less than 1600 picomoles of polyamines to make a therapeutic food designed to combat a syndrome or a pathology in which the NR2-B sub-unit of the N-methyl-D-aspartate receptor is involved.

Please replace the paragraph appearing on page 5, lines 13-17 with the following amended paragraph:

Therefore, an embodiment of this invention is intended to cover a novel use of such food compositions, which is not obvious from prior art, namely to combat syndromes or pathologies in which the NR2-B sub-unit of the N-methyl-D-aspartate receptor is involved.

Please replace the paragraphs starting on page 6, line 21 and ending on page 7, line 22 with the following amended

paragraphs:

Therefore an embodiment of this invention could be used to treat these pathologies or syndromes.

Preferably, the composition used according to an embodiment of this invention contains less than about 400 picomoles/g of putrescine, less than about 400 picomoles/g of spermidine, less than about 400 picomoles/g of spermine and less than about 400 picomoles/g of cadaverine.

Preferably, the composition used according an embodiment of to this invention contains less than about 400 and preferably less than about 200 picomoles/g of polyamines.

Advantageously, the composition used according to an embodiment of this invention contains less than about 100, and preferably less than about 50 picomoles/g of putrescine, less than about 100 and preferably less than about 50 picomoles/g of spermidine, less than about 100 and preferably less than about 50 picomoles/g of spermine, and less than about 100 and preferably less than about 50 picomoles/g of cadaverine. This type of composition provides at least 17 times less putrescine, 40 times less cadaverine, 70 times less spermidine and 220 times less spermine daily than the natural human food with the lowest content of polyamines, but which nevertheless satisfy human nutritional needs.

According to one variant, the composition used according to an embodiment of this invention also includes 10 to 35% by dry weight of lipids, 8 to 30% of proteins, 35 to 80% of glucides, and up to 10% of a mix composed of vitamins, minerals and electrolytes, as a percentage of the total dry weight.

Please replace the paragraph appearing on page 8, lines 21-24 with the following amended paragraph:

The quantity of water used to make the composition used according an embodiment of to this invention is determined such

that the composition is more or less liquid and can easily be ingested by the patient.

Please replace the paragraph appearing on page 9, lines 1-5 with the following amended paragraph:

Preferably, the composition used according to an embodiment of this invention contains less than 100 picomoles/g of putrescine, less than 100 picomoles/g of spermidine, less than 100 picomoles/g of spermine and less than 100 picomoles/g of cadaverine.

Please replace the paragraph appearing on page 9, lines 9-14 with the following amended paragraph:

According to one interesting variant of the invention, the composition used according to this an embodiment of the invention is enriched with at least one inhibitor of intracellular synthesis of polyamines, with a content by weight not exceeding 15% of the total dry weight in the composition and preferably between 0.2% and 7% by weight.

Please replace the paragraph appearing on page 11, lines 6-12 with the following amended paragraph:

Thus, the use of a food composition according to an embodiment of the invention containing alpha-methylornithine as an inhibitor of the intracellular synthesis of polyamines, can reduce the exogenic input of polyamines by intestinal bacteria without using an antibiotherapy concomitantly with administration of this composition, or at least by reducing the administered dose of antibiotics.

Please replace paragraph appearing on page 11, line 18 to page 12 line 2 with the following amended paragraph:

According to one variant, use of the composition according to an embodiment of the invention is enriched with vitamins, particularly vitamins added by intestinal bacteria in a healthy human. The antibiotherapy that can accompany administration of the said composition may also reduce the input of some vitamins. In this case, it may be necessary to enrich the composition used in these vitamins in order to avoid provoking a vitamin shortage following prolonged administration of the said composition. In particular, it may be useful to enrich the vitamins or vitamin derivatives in the composition. Some derivatives of vitamin A (retinoic acid) are inhibitors of the ODC activity.

Please replace the paragraph appearing on page 12, lines 21-23 with the following amended paragraph:

According to one variant of the invention, the composition used according to an embodiment of this invention forms a daily food ration for a human being and includes:

Page 14, after line 18, insert the following heading:

BRIEF DESCRIPTION OF THE DRAWINGS

Page 14, after line 28, insert the following heading:

DETAILED DESCRIPTION OF ILLUSTRATIVE EMBODIMENTS

Please replace the paragraph on page 19, lines 19-22 with the following amended paragraph:

It might be thought that, due to the use of polyamine-poor compositions according to an embodiment of the invention, it will be possible to restore the analgesic effect of opioid substances such as morphine in man.

Please replace the paragraph on page 20, lines 21-27 with the following amended paragraph:

By reducing the hypersensitivity to pain component related to phosphorylation of the NR2B sub-unit of NMDA receptors, and without eliminating the pain itself, polyamine-poor compositions according to an embodiment of the invention can be used in the context of non-invasive nutritional therapies capable of improving control over different types of painful syndromes in the long term.

Please add the following paragraphs on page 20, after line 27:

An embodiment of this invention proposes an alternative to the use of such antagonists to efficiently inhibit functioning of the NR2B sub-unit of NMDA receptors, in other words without inducing any major undesirable effect.

Thus, an embodiment of this invention proposes a therapeutic agent that could be used to treat neuro-degenerative diseases induced by stimulation of this sub-unit.

Another purpose of an embodiment of this invention is to propose a therapeutic agent capable of blocking the development of increased sensitivity to pain, memorisation of pain and consequently the development of chronic pain.

In particular, an embodiment proposes a therapeutic agent capable of restoring the analgesic effects of opioid substances by opposing the tolerance process.

Opioids such as morphine are powerful and widely used analgesics. However, they also cause dose-dependent development of hypersensitivity to pain in the long term (so-called pronociceptive effect) that can cause long-term hyperalgesia (exaggerated painful sensation to a nociceptive stimulus) and allodynies (painful sensation to a non-nociceptive stimulus).This increase in sensitivity to pain may be caused by the development of tolerance to analgesic effects (Simonnet et al., NeuroReport, 2003, 14, 1-7).

Although the present invention has been described with

reference to preferred embodiments, workers skilled in the art will recognize that changes may be made in form and detail without departing from the spirit and scope of the invention.